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Effects of menstrual cycle phases on preoperative anxiety: A randomized prospective observational trial

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Abstract

Aim: Women experience physical and psychological changes as a result of their menstrual cycle. This study aimed to investigate whether the menstrual cycle had any effect on the preoperative anxiety experienced by women who were scheduled to have an operation. Material and Method: One hundred female patients who were scheduled to undergo a septorhinoplasty, and who met the inclusion criteria, were enrolled in the present study. The patients were divided into two groups according to the phase of their menstrual cycle: Group F (follicular phase) and Group L (luteal phase). The patients' anxiety level was measured preoperatively using the State-Trait Anxiety Inventory Scale. The patients' heart rate and blood pressure measurements were performed preoperatively as well as at 1 min, 5 min, and 10 min after intubation. Results: The preoperative anxiety scores of the patients in the luteal phase (41.14) were statistically significantly higher than those of the patients in the follicular phase (36.04). The blood pressure, heart rate, and peripheral oxygen saturation values were found to be similar between the two groups. Discussion: We believe that preoperative anxiety is higher during the luteal phase of the menstrual cycle than during the follicular phase, but the hemodynamic data were similar in both phases.

Keywords

Anesthesia; General Anesthesia; Follicular Phase; Luteal Phase; Menstrual Cycle; Preoperative Anxiety

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Introduction

Preoperative anxiety is a condition that can negatively affect anesthesia, surgery, and postoperative recovery [1]. In fact, it has been shown that preoperative anxiety affects patients in both cognitive and physiological ways. If such anxiety is not correctly managed, it may lead to surgical procedures being postponed or canceled, or it may result in delayed postoperative wound healing. Anxiety can arise for a number of reasons, including a patient's concern about his/her health and surgery, uncertainty regarding possible outcomes, fear of not waking up after surgery, and fear/experience of pain. It has been suggested that preoperative anxiety might be experienced by as many as 80% of patients [2,3]. It has also been reported that anxiety directly increases a patient's blood pressure and changes his/her pulse rate, which might lead to hemodynamic instability during anesthesia [4,5].

The menstrual cycle is a physiological event accompanied by fluctuations in certain hormones, including estrogen and progesterone [6]. The menstrual cycle involves two basic phases, namely the follicular phase and the luteal phase [7]. Hormonal, physical, and psychological changes occur in women as a result of the menstrual cycle. Hence, it has been suggested that there is a strong relation between the menstrual cycle and an individual's emotional state [8]. It has previously been established that women feel well during the first phase of the menstrual cycle, while they face emotional, physical, and behavioral difficulties toward the end of the cycle [9]. Indeed, studies have shown that women experience anxiety, dysphoric discomfort, irritability, mood changes, depression, anger, and sleep disorders prior to menstruation [10,11]. In addition, the hemodynamic response might increase, depending on the physiological and psychological stress condition, during the luteal phase [12].

Various studies have been conducted with regard to the physiological and hemodynamic effects of the menstrual cycle. However, the effects of the different phases of the menstrual cycle on preoperative anxiety have not yet been investigated to an adequate extent. The present study hypothesizes that preoperative anxiety will vary according to the phases of the menstrual cycle.

The aim of this study was hence to investigate the effects of the different phases of the menstrual cycle on preoperative anxiety in patients scheduled to have surgery.

Material and Methods

The present study was conducted among patients who were scheduled to undergo a septorhinoplasty. All prospective septorhinoplasty patients who attended the hospital for a routine preoperative examination were informed about the study. After ethical approval had been received (Ethics Committee IRB Approval Date: 17 Jan 2018, Decision number: 02) and written informed consent had been obtained from the patients, the study was initiated. After the clinical trial had been recorded, the cases were started (NCT03708679).

Inclusion criteria for the study

Patients who did not smoke, did not drink alcohol, and did not use oral contraceptives; who did not report any irregular menstrual cycles (28±2-day menstruation cycle); who were between 18 and 45 years of age; and who were considered to be in the American Society of Anesthetics (ASA) I-II Group were included in the study.

Exclusion criteria for the study

Patients who were determined to exhibit difficulties in communication; who reported experiencing amenorrhea, pregnancy, delirium, psychological diseases, and major depressive disorders; who had malignancy and acute kidney failure; and who were older than 45 years of age were excluded from the study.

Groups

Information regarding their menstrual cycles was obtained from all the patients. The length (days) of the menstrual cycle was counted from the first day of the last cycle. Those patients who were found to be between the 8th and 12th days of the menstrual cycle were enrolled in Group F (follicular phase), while those who were found to be between the 20th and 24th days of the menstrual cycle were enrolled in Group L (luteal phase) [13]. The follow-up of the cases and the recording of the measurements were carried out by an anesthesiologist who was unaware of the patient groups.

Study procedure

The ages, heights, weights, and ASA scores of the patients were recorded while they were in the preoperative unit. The patients were divided into groups based on the dates of their last menstrual cycles. Standard monitoring procedures were used with all the patients, including electrocardiogram (ECG), heart rate (HR), non-invasive blood pressure (NIBP), and peripheral oxygen saturation (SpO2). After 10 minutes of resting, the patients' hemodynamic measurements were recorded at both the 5th and 10th minutes post-resting. Instant anxiety measurements were also performed. For this, the State-Trait Anxiety Inventory for AdultsTM (STAI-AD) [14] scale was used. When using this scale, scores of between one and four are awarded for each of the 20 included statements. The sum of the points awarded with regard to positive feelings (statements 1, 2, 5, 8, 10, 11, 15, 16, 19, and 20) was subtracted from the sum of the points awarded with regard to negative feelings (statements 3, 4, 6, 7, 9, 12, 13, 14, 17, and 18), with the resultant figure then being multiplied by a constant of 50. The scores for all the patients were added together to obtain the overall STAI-AD scores for the groups (Figure 1).

The standard monitoring process continued after the patients were transferred to the operating room. The patients' values were recorded before and after the induction of anesthesia, and again at the 1st, 5th, and 10th minutes after intubation. The venous vein was opened using a 20 G i.v. cannula. Then, 1 mg/kg of lidocaine, 2 µg/kg of fentanyl, 2 mg/kg of propofol, and 0.6 mg/kg of rocuronium were administered to induce anesthesia. If a maintenance dose was required, 0.5 mcg/kg of fentanyl, 0.2 mg/kg of rocuronium, and 1% of sevoflurane were used. Throughout the operation, 40% oxygen and 60% of medical air were used. The maintenance fluid required for the patients was provided with 0.9% NaCl. Once the procedure had been completed, the durations of both the surgery and the anesthesia were recorded.

Statistical analyses

The descriptive statistics concerning the investigated characteristics were expressed as the mean, standard deviation, minimum, and maximum values for the continuous variables, while they were expressed as the number and percentage for the categorical variables. The independent t-test was employed to compare the group means for the continuous variables. The

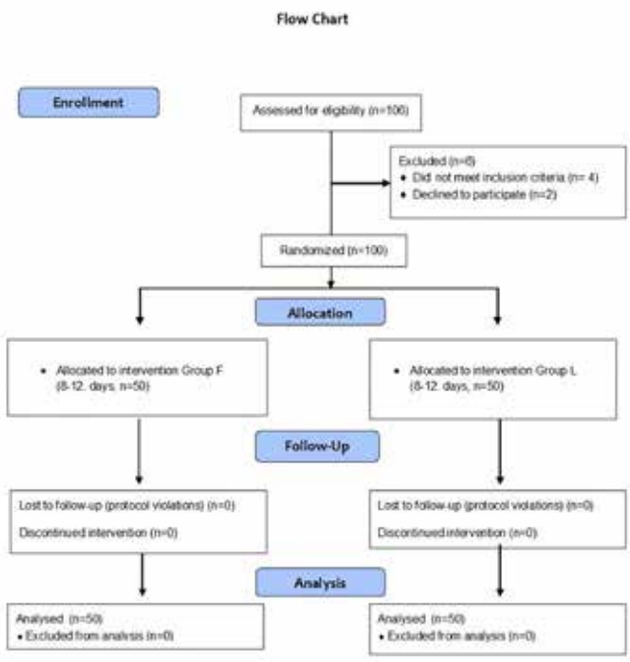

Figure 1. Study procedure.

Chi-Square test was employed to determine the relation between the groups and the categorical variables.

Based on the recommendations of previous studies [15-17], the standard deviation (σ) was considered to be 2.5 due to the number of anxiety scores (STAI-AD). The effect size (d) was assumed to be 0.9, while a Z value of 1.96 was used for the 0.05 type I error rate. The sample size was determined to be 45 by using the equation for sample size calculation ($n = Z^2.\sigma^2/d^2$), and 50 patients were included in each group. A p-value of <0.05 was considered to be statistically significant. Statistical Package for the Social Sciences (SPSS) v. 20.0 software (IBM SPSS for Windows, SPSS Inc., Chicago, IL, USA) was used to analyze the data.

Results

A total of 100 female patients were included in the present study. The patients' demographical data were found to be similar (p>0.05) (Table 1).

The mean anxiety score for Group L was determined to be statistically significantly higher than that for Group F (p<0.05) (Figure 2). The highest anxiety scores were found to be 71 in Group L and 50 in Group F, respectively.

No statistically significant differences were detected between the groups with regard to the systolic, diastolic, and mean blood pressures, heart rates or the peripheral oxygen saturation values (p>0.05). The average blood pressure values of the groups are shown in Table 2.

Table 1. Analysis of demographic data concerning the groups (values in mean±SD).

	Group F (n: 50)	Group L (n: 50)	Mean (n: 100)
Age (years)	25.64±5.72	25.38±5.41	25.51±5.54
Weight (kg)	56.54±7.52	59.42±9.51	57.92±8.65
ASA (I/II)	40/10	38/12	78/22
Menstrual cycle time (days)	28.2±1.32	28.82±1.41	28.51±1.06
Menstruation period (days)	5.41±1.16	5.63±0.75	5.52±0.93
Duration of surgery (min)	94.48±10,38	93.6±8,27	94.04±9.35
Duration of anesthesia (min)	107.46±10.99	106.16±8.93	105.87±13.70

Note: Analysis performed using the unpaired student's t-test. * p<0.05, ** p<0.01, *** p<0.001. ASA: American Society of Anesthesiologists

Figure 2. STAI-AD scores for the groups.
** Significant compared to Group F, p <0.01

Discussion

This study showed that the level of preoperative anxiety was higher in the septorhinoplasty patients who were in the luteal phase of their menstrual cycle. However, it was also determined that the blood pressure, heart rate, and peripheral oxygen saturation values were similar between the two groups. Our findings are consistent with those of previous studies, which reported higher levels of anxiety during the luteal phase of the menstrual cycle [6,7,18].

Premenstrual stress, which is observed during the luteal phase of the menstrual cycle, is characterized by physical, psychological, and behavioral changes, which are believed to affect 75% of women of reproductive age [19]. Previous studies have suggested that the functioning of the autonomic nervous system

Table 2. Comparison of the systolic, diastolic and mean blood pressure between the groups (values in mean±SD).

		N	Systolic BP	Diastolic BP	Mean BP
Preoperative 10 min	Group F	50	121.44±12.95	65.42±6.69	84.09±6.42
	Group L	50	124.34±13.18	65.18±5.59	84.90±6.11
	Mean	100	122.89±13.08	65.30±6.13	84.49±6.25
Preoperative 5 min	Group F	50	117.16±12.27	65.66±5.39	83.78±6.30
	Group L	50	121.64±12.02	66.58±5.41	84.97±5.77
	Mean	100	119.40±12.29	66.12±5.39	84.38±6.04
Before induction	Group F	50	114.96±11.95	63.58±6.08	80.70±6.41
	Group L	50	116.98±11.05	65.72±6.08	82.80±6.15
	Mean	100	115.97±11.50	64.65±6.14	81.75±6.34
After induction 1 min	Group F	50	103.38±18.37	59.02±8.47	73.80±8.75
	Group L	50	107.06±9.18	60.22±7.35	75.83±6.04
	Mean	100	105.22±14.52	59.62±7.91	74.82±7.55
After TI 1 min	Group F	50	112.42±17.33	61.42±7.25	78.42±8.26
	Group L	50	109.02±13.96	61.28±8.64	77.19±9.25
	Mean	100	110.72±15.75	61.35±7.94	77.80±8.75
After TI 5 min	Group F	50	110.98±17.48	60.52±7.79	77.34±9.40
	Group L	50	106.64±13.0	58.08±10.06	74.26±9.58
	Mean	100	108.81±15.51	59.30±9.04	75.80±9.56
After TI 10 min	Group F	50	106.90±14.67	60.02±7.11	75.82±9.78
	Group L	50	105.86±12.66	58.52±10.58	74.04±11.33
	Mean	100	106.38±13.64	59.27±9.00	74.94±10.56

Note: Analysis performed using the unpaired student's t-test. * p <0.05, ** p<0.01, *** p<0.001.
TI: Tracheal intubation

during the luteal phase might be related to various psychosomatic and behavioral symptoms that occur during the premenstrual period [20].

Kanojia et al. [7] conducted a study among healthy young women, and they reported that the average anxiety score during the luteal phase (46.96) was higher than that during the follicular phase (40.64). In the present study, it was likewise determined that the level of preoperative anxiety was higher during the luteal phase than during the follicular phase. The results of our study are hence in line with those reported in the literature. These results are consistent with the notion of psychological changes being induced by stress and with the stress-related psychological changes reported to occur during the luteal phase of the menstrual cycle. Similar to the present study, Gonda et al. [18] investigated the fluctuations in psychological symptoms that occur during the menstrual cycle. They determined that the anxiety level during the luteal period was higher than that during the follicular period. According to the utilized measurement scales, they detected psychological fluctuations, at least to some degree, in all participants. The fact that all our patients were scheduled to undergo aesthetic surgeries might have influenced both the anxiety measurements and hemodynamic reflections. The hemodynamic effects might differ in relation to different surgeries.

The luteal stage, during which the estrogen and progesterone hormone levels decrease, is associated with high irritability and negative mood. Thus, ovarian steroids are considered to be important predictors of fluctuations in women's moods during the menstrual cycle [21]. However, several prior studies have reported there to be no change in women's moods during the luteal phase [22,23]. Natale et al. [24] considered that this difference might be due to the scales employed in such studies. For instance, Redei et al. [25] directly compared the daily hormone measurements and the reported moods of women, and they concluded that there was no relation between the estradiol and progesterone levels and women's moods. Schwartz et al. [26] measured the daily ovarian hormone levels in women and reported that women's moods were not related to their hormone levels. They also reported that individuals' stress level and physical health status exerted a major impact on their mood, although fluctuations in ovarian hormones had little effect. In our study, while there were differences in the anxiety scores between the groups, the blood pressure, heart rates, and peripheral oxygen saturation values were not found to differ. This caused us to consider that the increased anxiety scores did not reach a level that might affect the hemodynamics during the luteal phase. In addition, the fact that the participants in our study were young and healthy individuals might also have influenced their hemodynamic stability. It is likely that different results would be found in older individuals and those with comorbidities.

Hemodynamic changes might also be observed during different phases of the menstrual cycle due to the effect of the hormones secreted during those phases [6,13]. In previous studies, it has been reported that the plasma norepinephrine levels and sympathetic activity in healthy women were found to be higher during the luteal phase than during the follicular phase [13,27]. It has also been reported that there were higher systolic blood pressure levels, as well as lower diastolic blood pressure levels, during the luteal phase due to the physiological and psychological stress that occurs during that phase impacting the hemodynamic response [12]. In our study, however, we did not find any differences between the patients' systolic, diastolic, and mean blood pressures. This difference might be due to the fact that our patients were all healthy and young individuals. Further, our patients were all ASA I-II patients, and they did not have any comorbidities. Similar to our study, Kanojia et al. [7] reported that the menstrual cycle only affected participants' hemodynamics to a minimal extent, while Gonda et al. [18] did not report any hemodynamic changes related to the different phases of the menstrual cycle.

Various studies have investigated the effects of the menstrual cycle on anesthesia, traumatic intubation, and the hemodynamic response to laryngoscopy. Hanci et al. [13] reported that the heart rates and blood pressures that were measured one minute after intubation were significantly higher in those patients who were in the luteal phase than in patients who were in the follicular phase. They reported that the altered hemodynamic responses observed in the face of intubation during the different menstrual cycle phases (rate pressure product [RPP]) might be associated with the increased response to plasma norepinephrine levels and sympathetic activity seen during the luteal phase. Khan et al. [28], however, reported that they detected more stable hemodynamic responses during the luteal phase. They also detected higher blood pressures and lower heart rates during the follicular phase. Hence, they recommended that any required surgeries should be scheduled during the luteal phase [28]. Yet, in a meta-analysis, it was reported that the current evidence is inadequate to determine the most appropriate phase of the menstrual cycle (luteal or follicular) during which to schedule anesthesia and surgery. The authors, therefore, stated that further randomized clinical trials were needed [29].

Limitations of the study

It must be acknowledged that the present study did have a number of limitations. The fact that the majority of patients were in the third decade of life might have had an impact on the finding of similar hemodynamic results. Further, we were unable to measure the patients' estrogen and progesterone levels in the present study. The inability to evidence the accuracy of the patients' menstruation phases using hormonal parameters hence represents another limitation of the study.

As a result, based on the results of the present study, we believe that the level of preoperative anxiety is higher during the luteal phase of the menstrual cycle than during the follicular phase, but the hemodynamic data were similar in both phases. However, more randomized studies are required to confirm our results.

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Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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